Claims 2, 4, 5, 8, 10, 24, 26, 29, 30, 40, 42 and 43 have also been amended to clarify the claimed subject matter and to correct minor informalities. Claim 19 has been amended to remove the specific recitation of SEQ ID NOs:21, 23 and 26 without prejudice and with the intent that specific recitation of these SEQ ID NOs may be reintroduced in this or a subsequently filed continuation or divisional patent application.

Applicants submit that no new matter is introduced by these amendments.

RESPONSE

Response to Restriction Requirement

Applicants initially would like to thank Examiner Einsmann for her time on February 28, 2002. As discussed with Examiner Einsmann at that time, Applicants provisionally elected with traverse to prosecute Group I, *i.e.*, claims 1-5, 8, 10-12, 19-20, 24, 26, 29-30, 40, 42 and 43.

The outstanding Office Action requires restriction under 35 U.S.C. § 121 between:

Claims 1-5, 8, 10-12, 19-20, 24, 26, 29-30, 40, 42 and 43, drawn to methods for detection of a non-viral organism, classified in class 435, subclass 6; and

Claims 44 and 50, drawn to kits for detecting a non-viral organism, classified in class 536, subclass 24.32.

Applicants, hereby, confirm that they wish to elect with traverse to prosecute Group I, *i.e.*, claims 1-5, 8, 10-12, 19-20, 24, 26, 29-30, 40, 42 and 43.

Amendments to the Specification

In accordance with Examiner recommendations and MPEP § 608.01, Applicants have deleted the embedded hyperlink and/ or other form of browser-executable code on page 14.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-5, 8, 10-12, 19-20, 24, 26, 29-30, 40, 42 and 43 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

According to the Office Action, claims 1-5, 8, 10-12, 19-20, 24, 26, 29-30, 40, 42 and 43 are indefinite for failing to recite a final process step which agrees back with the preamble. In response and in accordance with Examiner's recommendations, Applicants amend claim 1 to recite the step of

"detecting hybridization of the nucleic acid probe to SRP RNA, wherein hybridization of the probe is indicative of the presence of a non-viral organism from the group." Similarly, Applicants amend claim 20 to recite the step of "detecting the hybridization of the gel-immobilized nucleic acid probe to the duplex SRP RNA, wherein the hybridization of the gel-immobilized nucleic acid probe is indicative of the presence of a non-viral organism from the group." Applicants submit that these amendments render the claims sufficiently definite by reciting a final process step which agrees back with the preamble.

According to the Office Action, claims 1-5, 8, 10-12, 19-20, 24, 26, 29-30, 40, 42 and 43 are indefinite over the recitation of "substantially complementary" because the claims and the specification fail to provide a clear definition of this term or a method for determining such a level of complementarity. In response, Applicants have amended independent claims 1 and 20 to recite a "nucleic acid probe capable of specifically hybridizing to a subsequence..."

Claims 4, 5, 20, 24, 26, 29, 30, 42 and 43 were rejected as being indefinite over the recitation "stringent conditions" because it is not clear what limitation the Applicants are intending to impart. In response, Applicants have amended base claims 4, 20 and 26 (and the corresponding dependent claims) by deleting the references to "stringent conditions."

According to the Office Action, claims 26, 29, 30, 42 and 43 are indefinite over the recitation "the nucleic acid probe" because independent claim 20 recites two different nucleic acid probes. In response, Applicants have amended claim 20(i) and (ii) to recite "first nucleic acid probe" in order to distinguish this "first nucleic acid probe" from the second "gel-immobilized nucleic acid probe." In addition, dependent claims 26, 29, 30, 42 and 43 have been amended to recite "the first nucleic acid probe" as appropriate.

According to the Office Action, claim 24 is indefinite because it is unclear which "step of contacting" is meant as independent claim 20 has two separate contacting steps. In response, Applicants have amended claim 20(iii) to read "introducing the sample..." As amended, claim 20 has only one contacting step.

According to the Office Action, claim 40 is indefinite because it depends from a cancelled claim. In response, Applicants have amended claim 40 to render it dependent of claim 20.

According to the Office Action, there is insufficient antecedent basis for the limitation "the adaptor" in line 1 of claim 43, which is dependent of claim 26. In response, Applicants have amended

claim 43 to recite "the adaptor probe" for which Applicants submit there is sufficient antecedent basis in claim 26.

Applicants submit that amended claims 1-5, 8, 10-12, 19-20, 24, 26, 29-30, 40, 42 and 43 are sufficiently clear and definite to satisfy the requirements of 35 U.S.C. § 112, second paragraph. Applicants respectfully request that all the rejections under 35 U.S.C. § 112, second paragraph be reconsidered and withdrawn.

The Rejections Under 35 U.S.C. § 112, First Paragraph

According to the Office Action, claim 40 was rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification so as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Specifically, claim 40 was rejected for failing to disclose sequences of SRP RNA for certain genus's of bacterium.

Applicants respectfully submit that the proper standard under 35 U.S.C. §112, first paragraph, is whether one skilled in the art could make and use the invention without undue experimentation based on the disclosure in the patent application coupled with information known in the art. Applicants further submit that the specification as filed provides methods for detecting SRP RNA from numerous bacterial species. See, *inter alia*, Examples I and IV on pages 24-25 and 27-29 of the specification, respectively. Applicants submit that Examples I and IV include methods for detecting SRP RNA from species that were not listed in the Office Action as being available in the prior art. Therefore, Applicants submit that one of ordinary skill in the art could practice the presently claimed invention without undue experimentation. Accordingly, Applicants respectfully request that the rejection of claim 40 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

According to the Office Action, claim 19 was rejected under 35 U.S.C. § 112, first paragraph, for failing to provide enablement for methods which utilize nucleic acid probes comprising SEQ ID NO:21, SEQ ID NO:23 and SEQ ID NO:26. According to the Office Action, the practice of claim 19 utilizing probes comprising these sequences would require undue experimentation. In response, without acquiescing to this rejection, Applicants have amended claim 19 to recite those sequences for which the Examiner has acknowledged that sufficient enablement exists. Therefore, Applicants submit that this rejection is obviated and respectfully request the rejection of claim 19 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

Therefore, Applicants respectfully request that all the rejections under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

The Rejections Under 35 U.S.C. § 103(a)

Hogan et al. in view of Nakamura et al.

Claims 1-2, 4-5, 8, 10, 12 and 19 were rejected under 35 U.S.C. § 103(a) as being obvious, and thus unpatentable, over Hogan *et al.* (USPN 5,595,874) in view of Nakamura *et al.* (Nucleic Acids Research 20(19): 5227-5228). Applicants respectfully submit that a proper 35 U.S.C. § 103(a) rejection requires that the combination of cited references teach all of the claimed elements. However, Applicants respectfully submit that Hogan, in view of Nakamura, fails to disclose or enable all of the elements of the present claims. Therefore, the combined references cannot form the basis for a continued rejection under 35 U.S.C. § 103(a).

Specifically, Applicants respectfully submit that the combined art of Hogan and Nakamura fails to teach or enable the steps of electrophoresing the sample through an electrophoretic medium comprising immobilized nucleic acid probes. While Hogan reports the use of probes "in a hybridization assay to determine the presence or amount of rRNA from particular target non-viral organisms...," Hogan does not teach a method of detecting non-viral organisms by electrophoresing the sample through an electrophoretic medium. Similarly, although Nakamura reports sequences of SRP RNA for species of Bacillus, Nakamura does not teach the general concept of detecting the presence of non-viral organisms, or the electrophoresis step for hybridization.

Therefore, Applicants respectfully submit that even if one of ordinary skill in the art were to combine the disclosure of Hogan with that of Nakamura, one would not have taught all the elements of the pending claims as amended. Applicants respectfully submit that none of the cited references, alone or in combination, teach or suggest using electrophoresis to hybridize SRP RNA with immobilized nucleic acid probes. Accordingly, there can be no obviousness when at least one of the claimed elements is missing and is not suggested in any cited reference. Accordingly, Applicants respectfully submit that Hogan and Nakamura cannot form the basis for continued rejection under 35 U.S.C. § 103(a). Therefore, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Hogan et al. in view of Griffin

Claims 1-2, 4-5, 8, 10-12 and 19 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hogan *et al.* in view of Griffin (Journal of Biological Chemistry (1975) 250(14): 5426-5437). Applicants respectfully submit that neither reference teaches or enables the step of electrophoresing a sample containing SRP RNA through an electrophoretic medium comprising immobilized capture probes. As discussed above, where combined references fail to disclose all the limitations of the pending claims, a 35 U.S.C. § 103(a) rejection for obviousness is not appropriate. As discussed above, Hogan fails to teach the step of electrophoresing recited in the pending claims as amended. While Griffin reports the isolation and characterization of the 4.5 S RNA from *E. coli*, Griffin fails to teach or disclose the concept of electrophoresis for hybridization of SRP RNA with immobilized capture probes. Applicants respectfully submit that the combined art of Hogan and Griffin fail to disclose all elements of the pending claims as amended, and thus cannot form the basis of a 35 U.S.C. § 103(a) rejection.

Hogan et al. in view of Larsen et al.

Claims 1-2, 4-5, 8, 10-12 and 19 were rejected under 35 U.S.C. § 103(a) as being obvious, and thus unpatentable, over Hogan *et al.* in view of Larsen *et al.* (Nucleic Acids Research 19(2) 209-215). Applicants respectfully submit that the combined references fail to disclose, teach or enable the electrophoresis step to detect SRP RNA of non-viral organisms in a sample. As discussed above, Hogan *et al.* fails to teach or enable the step of electrophoresis. Furthermore, Larsen *et al.* reports the sequences of SRP RNA from 39 species of organisms. However, Larsen also fails to teach the electrophoresis step with immobilized nucleic acid probes as recited in the pending claims as amended. Applicants respectfully submit that a proper 35 U.S.C. § 103(a) rejection requires that the combined references must disclose all elements of the present claims. Where Hogan in view of Larsen fails to disclose the step of electrophoresing the sample, the combined references cannot form the basis for continued rejection under 35 U.S.C. § 103(a).

Hogan et al. in view of Nakamura et al., and further in view of Rudert et al.;
Hogan et al. in view of Griffin, and further in view of Rudert et al.; and
Hogan et al. in view of Larsen et al., and further in view of Rudert et al.

Claim 3 is rejected under 35 U.S.C. § 103(a) as being obvious, and thus unpatentable, over either (a) Hogan *et al.* in view of Nakamura *et al.* as applied to claims 1-2, 4-8, 10, 12 and 17-19, and further in

view of Rudert *et al.* (USPN 5,683,872), (b) Hogan *et al.* in view of Griffin as applied to claims 1-2, 4-8, 10-12 and 17-19, and further in view of Rudert *et al.*, or (c) Hogan *et al.* in view of Larsen *et al.* as applied to claims 1-2, 4-8, 10-13 and 17-19, and further in view of Rudert *et al.* Applicants submit that the three sets of combined references fail to disclose the step of electrophoresis of the sample for hybridization of SRP RNA and immobilized capture probes. As discussed above, Hogan, Nakamura, Griffin and Larsen all fail to teach electrophoresis as the means of detection. While Rudert reports "a method of detecting nucleic acid sequences in which polymers of selected oligonucleotide probes which are complementary to a region in a nucleic acid sequence that is to be detected are bound to a substrate," Rudert does not teach electrophoresis techniques. Applicants respectfully submit that where the combined references fail to disclose all the elements of the pending claims as amended, the combined references cannot form the basis for a continued rejection under 35 U.S.C. § 103(a).

Hogan et al. in view of Nakamura et al., and further in view of Ghosh et al.

Claims 20, 24, 29-30 and 40 were rejected under 35 U.S.C. § 103(a) as being obvious, and thus unpatentable, over Hogan *et al.* in view of Nakamura *et al.* as applied to claims 1-2, 4-5, 8, 10, 12 and 19 above, and further in view of Ghosh *et al.* (USPN 5,237,016). As above, Applicants respectfully submit that this combination of references fails to disclose electrophoresing the sample through a medium comprising immobilized nucleic acid probe as a means to hybridize and detect SRP RNA. As discussed above, both Hogan and Nakamura fail to teach electrophoresis and immobilized nucleic acid probe techniques. While Ghosh reports "methods and means for covalent attachment of oligonucleotides to solid supports substantially at their 5'-ends," Ghosh fails to teach the step of electrophoresing samples through an electrophoretic medium comprising immobilized nucleic acids probes. Therefore, the combination of references fails to disclose each element of the pending claims as amended and, thus, cannot form the basis of a 35 U.S.C. § 103(a) obviousness rejection.

Hogan et al. in view of Griffin, and further in view of Ghosh et al.

Claims 20, 24, 30 and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hogan *et al.* in view of Griffin as applied to claims 1-2, 4-5, 8, 10-12 and 19 above, and further in view of Ghosh *et al.* As discussed above, each of these references fails to disclose the elements of electrophoresing a sample through a medium comprising immobilized nucleic acid probes. Where the combined references of Hogan, Larsen and Ghosh fail to disclose each element of the pending claims as amended, they cannot form the basis of a proper 35 U.S.C. § 103(a) obviousness rejection.

Hogan et al. in view of Larsen et al., and further in view of Ghosh et al.

Claims 20, 24, 29-30 and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hogan *et al.* in view of Larsen *et al.* as applied to claims 1-2, 4-5, 8, 10-12 and 19 above, and further in view of Ghosh *et al.* As discussed above, each of these references fails to disclose the elements of electrophoresing a sample through a medium comprising immobilized nucleic acid probes. Where the combined references of Hogan, Larsen and Ghosh fail to disclose each element of the pending claims as amended, they cannot form the basis of a proper 35 U.S.C. § 103(a) obviousness rejection.

Hogan et al. in view of Nakamura et al., and further in view of Ghosh et al.;
Hogan et al. in view of Griffin, and further in view of Ghosh et al.; and
Hogan et al. in view of Larsen et al., and further in view of Ghosh et al.

Claim 26 was rejected under 35 U.S.C. § 103(a) as being obvious, and thus unpatentable, over either (a) Hogan *et al.* in view of Nakamura *et al.* as applied to claims 20, 24, 29-30 and 40, and further in view of Ghosh *et al.*, (b) Hogan *et al.* in view of Griffin as applied to claims 20, 24, 30 and 40, and further in view of Ghosh *et al.*, or (c) Hogan *et al.* in view of Larsen *et al.* as applied to claims 20, 24, 29-30 and 40, and further in view of Ghosh *et al.* As discussed above, each of these five references fails to disclose the elements of electrophoresing a sample through a medium comprising immobilized nucleic acid probes. Where all three sets of the combined references fail to disclose each element of the pending claims as amended, none can form the basis of a proper 35 U.S.C. § 103(a) obviousness rejection.

Applicants respectfully submit that each set of combined references cited above fails to teach or enable each element of the pending claims as amended. Applicants respectfully submit that none of the combined references can form the basis for continued rejection under 35 U.S.C. § 103(a). Therefore, Applicants respectfully request that each and every rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

CONCLUSION

Applicants respectfully request that the rejections under 35 U.S.C. §§ 103 and 112 be withdrawn on the basis of the foregoing amendments and remarks. Applicants submit that pending claims 1-5, 8, 10-12, 19-20, 24, 26, 29-30, 40 and 42-43 are in condition for allowance, and request early favorable

action. Applicants respectfully request a telephonic interview with the Examiner prior to the issuance of a further Office Action. The Examiner is invited to contact the undersigned attorney for the Applicants.

Respectfully submitted,

Pat RH Waller

Date: September 18, 2001
Reg. No. 41, 418

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U.S. SERIAL NO. 10/024,944

MARKED-UP COPY OF AMENDMENTS TO THE CLAIMS

1. (Amended) A method for detecting in a sample a non-viral organism belonging to a group, the group consisting of at least one, but less than all non-viral organisms, the method comprising the steps of:

(i) introducing [contacting] a sample comprising SRP RNA into an electrophoretic medium comprising an immobilized [with a] nucleic acid probe capable of specifically hybridizing [, wherein the nucleic acid probe is substantially complementary] to a subsequence of SRP RNA from a [the] group of non-viral organisms;

(ii) subjecting the electrophoretic medium to an electric field such that [incubating] the sample comprising SRP RNA migrates through the medium and the immobilized nucleic acid probe [under hybridization conditions such that the nucleic acid probe] hybridizes to SRP RNA from the group of non-viral organisms but does not detectably hybridize to SRP RNA from other non-viral organisms that do not belong to the group; and,

(iii) detecting hybridization of the nucleic acid probe to SRP RNA, wherein hybridization of the probe is indicative of the presence of a non-viral organism from the group.

2. (Amended) The method of claim 1, wherein the immobilized nucleic acid probe comprises a detectable moiety.

4. (Amended) The method of claim 1, wherein [the] step (i) [of contacting] further comprises using [the use of] one or more additional immobilized nucleic acid probes capable of specifically hybridizing [that are substantially complementary] to a subsequence of SRP RNA from the non-viral organism [and have the ability to hybridize under stringent conditions to the SRP RNA from the non-viral organism].

5. (Amended) The method of claim 4, wherein one of the immobilized nucleic acid probes comprises a detectable moiety.

8. (Amended) The method of claim 1, wherein the immobilized nucleic acid probe is selected from the group consisting of DNA, PNA, and 2'-O-methyl RNA.

10. (Amended) The method of claim 1, wherein the immobilized nucleic acid probe is perfectly complementary to the subsequence of SRP RNA.

19. (Twice Amended) The method of claim 1, wherein the immobilized nucleic acid probe has a nucleotide sequence selected from the group consisting of: GCTGCTTCCTTCCGGACCTGAC (SEQ ID NO:2); GCTGCTTCCTTCCGGACCTGA (SEQ ID NO:3); GGCACACGCGTCATCTGC (SEQ ID NO:9); GCTGCTTCCTTC (SEQ ID NO:4); GCTGCTTCCTTCCGGACCTGAGTGAATACGTTCCCGGGCCT (SEQ ID NO:7);

GCTGCTTCCTTCCGGACCTGACAAAAACGATAAACCAACCA (SEQ ID NO:8); GCTGCTTCCTTCCGGACCTGACCTGGTAAA (SEQ ID NO:11); GCTGCTTCCTTCCG (SEQ ID NO:5); GACCTGACCTGGTA (SEQ ID NO:6); [GCTGCTTCCGTC (SEQ ID NO:21);] CGGACCTGACCTG (SEQ ID NO:22); [AGGACCUGACAUG (SEQ ID NO:23);] CGGACCUGACCAG (SEQ ID NO:24); and CGGACCUGACAAG (SEQ ID NO:25) [; and CGGAUCUGACACG (SEQ ID NO:26)].

20. (Amended) A method for detecting in a sample a non-viral organism belonging to a group, the group consisting of at least one, but less than all of non-viral organisms, the method comprising the steps of:

(i) contacting a sample comprising SRP RNA with a first nucleic acid probe capable of specifically hybridizing [, wherein the nucleic acid probe is substantially complementary] to a subsequence of SRP RNA from a [the] group of non-viral organisms [and wherein the nucleic acid probe has the ability to hybridize under stringent conditions to the SRP RNA from the group of non-viral organisms];

(ii) incubating the sample comprising SRP RNA and the first nucleic acid probe [under stringent hybridization conditions] to form a duplex SRP RNA from the group of non-viral organisms;

(iii) introducing [contacting] the duplex SRP RNA into an electrophoretic medium comprising [with a] a gel-immobilized nucleic acid probe capable of specifically hybridizing [, wherein the gel-immobilized nucleic acid capture probe is substantially complementary] to a subsequence of the duplex SRP RNA from the group of non-viral organisms;

(iv) subjecting the electrophoretic medium to an electric field such that [incubating] the duplex SRP RNA migrates through the medium and the gel-immobilized nucleic acid probe [under hybridization conditions such that the gel-immobilized nucleic acid probe] hybridizes to the subsequence of the duplex SRP RNA from the group of non-viral organisms, but does not detectably hybridize to SRP RNA from other non-viral organisms that do not belong to the group; and,

(v) detecting the hybridization of the gel-immobilized nucleic acid probe to the duplex SRP RNA, wherein the hybridization of the gel-immobilized nucleic acid probe is indicative of the presence of a non-viral organism from the group.

24. (Amended) The method of claim 20, wherein the step of contacting [with a nucleic acid probe] further comprises the use of one or more additional nucleic acid probes.

26. (Amended) The method of claim 20, wherein the first nucleic acid probe is an adaptor probe comprising a subsequence that hybridizes [under stringent conditions] to the gel-immobilized nucleic acid probe.

29. (Amended) The method of claim 20, wherein the first nucleic acid probe is about 15 to about 25 nucleotides in length.

30. (Amended) The method of claim 20, wherein the gel-immobilized nucleic acid probe and the first nucleic acid probe are selected from the group consisting of DNA, PNA, and 2-O-methyl RNA.

40. (Amended) The method of claim 20 [39], wherein the non-viral organism is a bacterium selected from the group consisting of *Propionibacterium* sp., *Klebsiella* sp., *Enterobacter* sp., *Serratia* sp., *Salmonella* sp., *Legionella* sp., *Pseudomonas* sp., *Haemophilus* sp., *Escherichia* sp., *Mycoplasma* sp., *Micrococcus* sp., *Listeria* sp., *Bacillus* sp., *Staphylococcus* sp., *Streptococcus* sp., *Clostridia* sp., *Neisseria* sp., *Helicobacter* sp., *Vibrio* sp., *Campylobacter* sp., *Bordetella* sp., *Ureaplasma* sp., *Treponema* sp., *Leptospira* sp., *Borrelia* sp., *Actinomyces* sp., *Nocardia* sp., *Chlamydia* sp., *Rickettsia* sp., *Coxiella* sp., *Ehrilichia* sp., *Rochalimaea* sp., *Brucella* sp., *Yersinia* sp., *Fracisella* sp., and *Pasteurella* sp.

42. (Amended) The method of claim 20, wherein the first nucleic acid probe has a nucleotide sequence selected from the group consisting of:
GCTGCTTCCTTCCGGACCTGAGTGAATACGTTCCCGGGCCT (SEQ ID NO:7); and
GCTGCTTCCTTCCGGACCTGACAAAAACGATAAACCAACCA (SEQ ID NO:8).

43. (Amended) The method of claim 26, wherein the adaptor probe has a nucleotide sequence selected from the group consisting of:
GCTGCTTCCTTCCGGACCTGAGTGAATACGTTCCCGGGCCT (SEQ ID NO:7); and
GCTGCTTCCTTCCGGACCTGACAAAAACGATAAACCAACCA (SEQ ID NO:8).

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MARKED-UP COPY OF AMENDMENTS TO THE SPECIFICATION

On the 14th page of the specification, please amend the first sentence of the first full paragraph starting at line 13 to read as follows:

Sequences for SRP RNA can be obtained through publicly available databases, *e.g.*, on the world wide web [at http://www.medkem.gu.se/dbs/SRPDB/], or GenBank database.